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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,417	09/26/2006	Shinzo Yasuda	04853.0138	2159

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,417	YASUDA ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/2006; 4/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-10 are pending. Claims 3-6 are amended by applicant. Claims 1-10 are under current examination.

Sequence Compliance

Sequence Listing and CRF have been received and are acknowledged by examiner. A statement that the Computer Readable Form (CRF) and the Sequence Listing are identical has been submitted and is acknowledged by examiner.

Oath/Declaration

The new oath or declaration, having the signatures of all inventors, received on 26 September 2006 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 11 May 2006 consisting of 3 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/JP05/05480 (filed 03/25/2005). This application also claims benefit from foreign patent applications JAPAN 2004-093417 (filed 03/26/2004) and JAPAN 2004-124524 (filed 04/20/2004). The instant application has been granted the benefit date, 26 March 2004, from the application JAPAN 2004-093417.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The embedded hyperlink is located on page 38, line 24.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the gene" in lines 1-3, 5-7. There is insufficient antecedent basis for this limitation in the claim. The first occurrence of a term should be

preceded by the words "a" or "an". In addition, there is insufficient antecedent basis for "the reactivation factor" in lines 4-5.

Claims 2-5 recite the limitation, "derived from Lactobacillus reuteri." It is unclear what "derived from" means. Clarification is required.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation, "the genes encoding aldehyde dehydrogenase," and the claim also recites "the gene encoding aldehyde dehydrogenase" (as from claim 1) which is the narrower statement of the range/limitation. If there was one gene in claim 1, how can

there not be more than one gene. Furthermore, there are other instances of the gene/genes issue in the claim. This could be a grammar issue, rather than a broad/narrow issue, but in either case, there is indefinite language in this claim.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (1) culturing cells, and (2) isolating the 1,3-propanediol and/or 3-hydroxypropionic acid.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention

is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement;* (Federal Register/Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claims 1-7 are broadly drawn such that they encompass a genus of "transformants." The specification does not specifically define the word, transformant. However, on page 16, lines 16-20, the specification states, "Transformants can be obtained by...introducing the resulting recombinant vector into a host." The specification states, "examples of such hosts include...bacteria...yeast...animal cells...and insect cells" (page 17, lines 10-16). The implication of this paragraph is that any microbe, mold, animal, plant, or insect which has been transformed with a foreign gene is a "transformant." The working examples of the instant specification only support enzymatic pathway engineering in bacteria, particularly *E.coli* and *Lactobacillus reuteri.*

Claims 8-9 are broadly drawn such that they encompass a genus of "knockout bacteria." The specification states, "In addition to bacteria of the genera *Lactobacillus, Salmonella, Klebsiella, Listeria, Clostridium, Escherichia, Enterobacter, Caloramator, Acetobacterium, Brucella, Flavobacterium, Fusobacterium, Citrobacter, and Propionibacteriurn*, bacteria comprising the pdu operon and the gene encoding phosphotransacylase, from which the gene encoding glycerol dehydrogenase is

knocked out, are also within the scope of this aspect." (page 22, lines 8-12). However, the specification describes their basis for this assertion as follows, "The present inventors discovered that knocking out of the gene encoding glycerol dehydrogenase from bacteria of the genus *Lactobacillus* comprising the pdu operon results in the production of 1,3-propanediol and 3-hydroxypropionic acid from glycerol, based on the mechanism shown in Fig. 2." (page 23, lines 22-25). It is clear that the working examples are directed to *Lactobacillus reuteri* comprising a knocked out gene encoding glycerol dehydrogenase. The instant application does not contain support for every knockout bacteria comprising the pdu operon and the gene encoding phosphotransacylase, from which the gene encoding glycerol dehydrogenase is knocked out. In addition, the specification does not contain support for knockout bacteria of the genera *Salmonella, Klebsiella, Listeria, Clostridium, Escherichia, Enterobacter, Caloramator, Acetobacterium, Brucella, Flavobacterium, Fusobacterium, Citrobacter, and Propionibacteriurn.*

Claim 10 claims to use the transformants and knockout bacteria of claims 1-9. Accordingly, the method of claim 10 contains the same written description problems and is likewise rejected.

Claims 1-7 are broadly drawn, such that they apply to a genus of transformants comprising nucleic acids that hybridizes under high stringency to various genes (glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase). The specification defines the genes for glycerol dehydratase by hybridization under stringent conditions (page 5).

The specification defines the genes for propanol dehydrogenase by hybridization under stringent conditions (page 6). The specification defines the genes for propionaldehyde dehydrogenase by hybridization under stringent conditions (page 9). The specification defines the genes for propionate kinase by hybridization under stringent conditions (page 9). The specification defines the genes for 1,3-propanediol oxidoreducatase by hybridization under stringent conditions (page 13). However, the working examples provided in the instant application only demonstrate nucleic acids from *Lactobacillus reuteri.*

The Revised Interim Guideline for Examination of Patent Applications under 35 USC § 112, p1 "Written Description" Requirement (Federal Register/ Vol 66. No 4, Friday January 5, 2001) states "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (column 2, page 71436, emphasis added).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED.*" (See page

1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize the [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

With respect to claims limiting a polynucleotide by hybridization conditions, even under relatively high stringent conditions, the claimed nucleotide sequence could hybridize to a genus of polynucleotides that are similar, but not identical to the recited polynucleotides. The limitation by hybridization is obviously generic to a considerable number of nucleotides varying in the length of the nucleic acids, the degree of homologies among the sequences, and the biological activities of the promoter, which may or may not be involved in the function of the genes cite above. This genus also embraces sub-sequences that are unknown and include unsequenced polynucleotides, whose function is yet to be determined.

Considering the potentially large numbers organisms comprising genetic mutations of polynucleotides encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed. In addition, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed genus of

"transformants" and "knockout bacteria" commensurate to its scope at the time the application was filed.

ENABLEMENT

Claims 1-7 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some 'experimentation.'" Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Nature of the Invention

The full scope of the claimed invention encompasses an enormous number of nucleic acids which could hybridize with glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. The size of these hybridizing nucleic acids might be small, or equal in size to full-length the particular genes, or larger than the particular genes. The nucleic acids might also encompass very large nucleic acids that hybridize under highly stringent conditions only over a short range near one end of both sequences. In this case, there would be a very low level of homology between the two sequences, despite high stringency hybridization.

With respect to claims limiting a polynucleotide by hybridization conditions, even under relatively high stringent conditions, the claimed nucleotide sequence could hybridize to a genus of polynucleotides that are similar, but not identical to the recited polynucleotides. The limitation by hybridization is obviously generic to a considerable number of nucleotides varying in the length of the nucleic acids, the degree of homologies among the sequences, and the biological activities of the encoded polypeptides, which may or may not be involved in the function of glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. This genus also embraces sub-sequences that are

unknown and include unsequenced polynucleotides, whose function is yet to be determined.

Working Examples and Guidance Provided

The specification indicates that any DNA which hybridizes to particular SEQ ID NOs recited on pages 5-6, 9 and 13 of the instant specification could be considered a homologue of the glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. There are no working examples of nucleic acids that have been isolated through the stringent hybridization method.

State of the Art and Analysis of the Issues

A skilled artisan would not know how to make a nucleic acid which corresponds to the large number of species of nucleic acid encompassed by Claims 1-7. Some of the nucleic acids that fit within the genus of Claims 1-7 would not be homologues of glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. In fact, despite hybridizing under high stringency conditions, these molecules would be structurally and functionally unrelated to the recited genes. Sequences which fit into this class of unrelated molecules would require further research in order for an artisan to learn how to use them. Furthermore, the artisan would have no reason to make such sequences.

Wolcott (CLINICAL MICROBIOLOGY REVIEWS, Oct. 1992, p. 370-386) teaches "hybridization...is subject to...nonspecific background interference" (page 372, column 1) and "hybridization studies...produced...false-positive reactions" (page 371, column 2). Walcott further teaches "short probes...are subject to more nonspecific hybridizations, are limited in specificity, and are more difficult to label....Long probes hybridize more stably than short probes at high temperatures and low salt concentrations (low stringency)." (page 371, column 2). Gress et al. (*Mammalian Genome 3:* 609-619, 1992) teach, "complex probes usually generate a high amount of background and unspecific hybridization." (page 610, column 1). The teachings of Wolcott and Gress et al. cast doubt on the homology of the sequences derived through hybridization methods. If sequences that hybridize under stringent conditions are not homologous or functionally related to those sequences of the genus of claim 16, then there is surely difficulty for the artisan to make and/or use these sequences. Or if the amount of relatedness of the hybridizing sequence to glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, or 1,3-propanediol oxidoreducatase only comprises a single domain, then the artisan would likewise encounter difficulty in using these sequences and would be required to perform further investigation to find a utility for these discovered sequences.

Therefore, the quantity of experimentation required to make and/or use the invention, as claimed, is insufficient to enable the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Dobrogosz et al (US-5,352,586, issued October 4, 1994).

Claims 1-5 are directed to transformants having various genes encoding glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. Claims 2-5 further limit claim1, by requiring that the genes be derived from *Lactobacillus reuteri.* The instant specification describes a transformant as comprising nucleic acids that hybridizes under high stringency to various genes (glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase). Dobrogosz et al. teach, *Lactobacillus reuteri* transformants comprising the genes for glycerol dehydratase (col.2, lines 61-62). The genes for propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase are intrinsic to the microorganism, *Lactobacillus reuteri,* since the endproducts of anaerobic glycerol metabolism are 1,3-propanediol and/or β-hydroxypropionic acid. Dobrogosz et al. teach culturing Lactobacillus reuteri

transformants in glycerol to produce 1,3-propanediol and/or β-hydroxypropionic acid (col.12, lines 40-42).

Claim 10 is directed to a method for producing 1,3-propanediol and/or 3-hydroxypropionic acid from culturing a recombinant microorganism in the presence of glycerol. Dobrogosz et al. teach culturing Lactobacillus reuteri transformants in glycerol to produce 1,3-propanediol and/or β-hydroxypropionic acid (col.12, lines 40-42).

Accordingly, Dobrogosz et al. anticipated the instant claims.

Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Skraly et al (US-6,329,183, issued 11 December 2001).

Claims 1 is directed to transformants having various genes encoding glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. Skraly et al. teach, "organisms that contain one or both dehydratases typically are able to convert glycerol to 3-hydroxypropionaldehyde to 1,3-propanediol" (col.5, lines 57-59) and "Because all the genes necessary to implement the production of poly(3-hydroxypropionate) from central metabolic intermediates via glycerol have been cloned and are available in genetically manipulatable for, any combination of plasmid-borne and integrated genes may be used and the implementation of this pathway is therefore not restricted to the schemes outlined herein. Many different implementations will be apparent to those skilled in the art." (col.5, lines 40-47).

Claim 10 is directed to a method for producing 1,3-propanediol and/or 3-hydroxypropionic acid from culturing a recombinant microorganism in the presence of glycerol. Skraly et al. teach "transgenic *Escherichia coli* synthesized...1,3-propanediol from glycerol" (col.7, lines 14-15). Skraly et al. also teach, "genetically engineered systems for the production...of 1,3-propanediol from glycerol" (col.6, lines 44-46).

Accordingly, Skraly et al. anticipated the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skraly et al (US-6,329,183, issued 11 December 2001) in view of Dobrogosz et al (US-5,352,586, issued October 4, 1994) and as evidenced by Omura et al (US2006/0063217).

The teachings of Skraly et al. and Dobrogosz et al. are cited above in the 35 USC 102 sections.

Skraly et al. does not teach the source of the genes cited in claims 2-5 as coming from *Lactobacillus reuteri.* Dobrogosz et al. does not particularly teach the knockout limitations of claims 6-9. Furthermore, both references to not specifically teach the use of the bacteria from the genera *Lactobacillus, Salmonella, Klebsiella, Listeria, Clostridium, Escherichia, Enterobacter, Caloramator, Acetobacterium, Brucella, Flavobacterium, Fusobacterium, Citrobacter, and Propionibacteriurn*, comprising a knock out of the gene encoding glycerol dehydrogenase.

Skraly et al., however, teach, "Because all the genes necessary to implement the production of poly(3-hydroxypropionate) from central metabolic intermediates via glycerol have been cloned and are available in genetically manipulatable for any combination of plasmid-borne and integrated genes may be used and the implementation of this pathway is therefore not restricted to the schemes outlined herein. Many different implementations will be apparent to those skilled in the art." (col.5, lines 40-47). Dobrogosz et al. list a variety of bacteria including *Lactobacillus , Salmonella, Clostridium, Escherichia* (col.9).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to culture recombinant bacteria in glycerol to produce 1,3-propanediol and/or 3-hydroxypropionic acid, using a variety of possible enzymatic alternatives in a variety of possible microorganisms.

The person of ordinary skill in the art would have been motivated to make those modifications because 1,3-propanediol and/or 3-hydroxypropionic acid are "industrially useful as polymers or as starting materials for a range of chemical intermediates " (Skraly, abstract).

The skilled artisan would have had a reasonable expectation of success in combining the teachings of Skraly et al. and Dobrogosz et al. because each of these references teach production of 1,3-propanediol and/or β-hydroxypropionic acid from glycerol using microorganisms. Dobrogosz et al. teach culturing Lactobacillus reuteri transformants in glycerol to produce 1,3-propanediol and/or β-hydroxypropionic acid (col.12, lines 40-42). Skraly et al. teach "transgenic *Escherichia coli* synthesized...1,3-propanediol from glycerol" (col.7, lines 14-15).

Therefore the method as taught by Skraly et al. in view of Dobrogosz et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott Long
Patent Examiner
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